TEST PLAN FOR Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo-
(CAS No. 37853-59-1)

OVERVIEW

Great Lakes Chemical Corporation agrees to sponsor Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo- (CAS No. 37853-59-1) under the Environmental Protection Agency's (EPA) High Production Volume (HPV) Chemical Challenge Program. The company hereby submits a test plan for this substance. It is the intent of the sponsoring company to use existing data to fulfill the Screening Information Set (SIDS) endpoints for environmental fate, ecotoxicity and human health effects.

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1. Introduction

Great Lakes Chemical Corporation submits this test plan for Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo- for hazard review under the Environmental Protection Agency High Production Volume Chemical Program. The technical contact at this company is:

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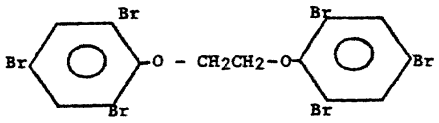
2. Designation of Test Substance

The test substance presented in this test plan is Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo-, CAS No. 37853-59-1. The chemical structure is as follows:



This chemical is also known as:

Benzene, (1,1'-[1,2-ethanediylbis(oxy)]bis[(2,4,6-tribromo-]) (Chemical Abstracts nomenclature) and 1,2-bis(2,4,6-tribromophenoxy)ethane.

The chemical is also sold under the trade names Firemaster 680 (FM 680) and Great Lakes FF-680, MC-680, and VC-680.

The primary use of this chemical is incorporation in resin or plastic as a flame retardant.

3. Criteria for Determining Adequacy of Data

All available studies were reviewed and assessed for adequacy according to the standards of Klimisch et al. (1997). Studies receiving a Klimisch rating of 1 or 2 were considered to be adequate. A test plan matrix that indicates if data are provided for each end point in the sets of robust summaries (see attachment) was constructed after a careful evaluation of all existing data (see below).

4. Discussion of Available Test Information

4.1 Chemical and Physical Properties

The results of chemical/physical property testing are shown in Table 1.

Table 1. Chemical/physical properties of Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo-,

Endpoint	Value
Melting point (° C)	224[a] 213.6[b]
Boiling point (° C)	ca. 502[b,c]
Vapor pressure (hPa at 25° C)	< .000001 [b]
Partition coefficient (Log Pow or Kow)	3.137[a] ca. 9.14[b]
Water solubility (mg/l at 25 ° C)	0.2 [a] 0.338[b]

[a] measured; [b] estimated by EPIWIN ; [c] at 1016 hPa

4.1.1 Melting Point

A melting point of 224ºC was measured following Directive 84/449/EEC, A.1 "Melting point/melting range" (Kirk-Othmer, 1993). In addition, a melting point of ca. 213.6° C was estimated using EPIWIN MPBPWIN (v1.40), using several methods. The estimated melting point selected is the weighted value of these methods.

4.1.2 Boiling Point

EPIWIN MPBPWIN (v1.40) estimates a boiling point of about 502° C at 1016 hPa.

4.1.3 Vapor Pressure

EPIWIN MPBPWIN estimates a vapor pressure of < .000001 hPa at 25° C.

4.1.4 Octanol/Water Partition Coefficient

A log Pow of 3.137 was measured (Yu and Atallah, 1977)) following the method described by Leo et al. (1971). A value of ca. 9.14 was estimated by EPIWIN KOWWIN (v1.66). Preference should be given to the measured value.

4.1.5 Water Solubility

A measured value of 0.2 mg/l (at 25 ° C) has been determined using ^{14}C labeled test substance (Yu and Atallah, 1978). The same study was used to determine solubilities of 0.16 mg/l at 15°C and 0.08 mg/l at 35°C. EPIWIN WSKOW (v1.40) estimates a value of 5.752 E-7 mg/l based on an estimated Log Kow of 9.14. As in the case with partition coefficients discussed above, it is likely that the measured values are more accurate than the estimated values. Altogether, the available data offer sufficient characterization for this end point to indicate limited water solubility.

4.1.6 Summary/Test Plan for Physical Properties

Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo- is a solid with a high melting point, very high boiling point, limited volatility and water solubility, and a 3.14 (measured) octanol/water partition coefficient. The available information for the required endpoints is sufficient to characterize the physical properties for the test substance for screening purposes. No additional testing is necessary.

4.2 Environmental Fate/Pathways

Results of environmental fate modeling and studies are summarized in Table 2.

Table 2. Environmental fate parameters for Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo-

Endpoint	Value
Photolysis (Atmospheric $T_{1/2}$)	9.6 hours[a]
Indirect Photolysis (OH sensitizer) (Hydroxyl Radical Rate Constant)[b] (Atmospheric $T_{1/2}$)[b]	 ca. 1.4857 x 10^{-11} cm^3/(molecule*sec) 8.6 hours
Stability in Water	No reliable measured or estimated data[c]
Biodegradation[a]	Not readily biodegraded
Henry's Law Constant[b]	4.25 x 10^{-7} atm-m^3/mol
Koc[b]	71800
Environmental transport (Fugacity Level III mass percentages)[b]	Air = 0.0675 Water = 1.17 Soil = 37.3 Sediment = 61.5

[a] Measured value
[b] Estimated using EPIWIN
[c] The test substance does not possess functional groups generally recognized to be readily hydrolyzable in water under neutral ambient conditions.

4.2.1 Photodegradation

A photodegradation half-life of 0.4 days (9.6 hours) has been measured by subjecting ^{14}C labeled test substance placed on a silica gel surface with uv radiation (Yu, 1979 . A hydroxyl radical-induced photodegradation rate constant of ca. 1.4857 x 10^{-11}cm3/(molecule*sec) has been estimated using EPIWIN AOP (v1.90). The same program estimates a half-life of 8.6 hours for photodegradation with hydroxyl radical as sensitizer. The strictly limited volatility of the test substance suggests that atmospheric photodegradation is not an important degradative pathway, although rapid photodegradation of the solid material would be expected on direct exposure to sunlight.

4.2.2 Stability in Water

A hydrolysis rate cannot be determined by the EPIWIN program. An available hydrolysis study indicates that hydrolysis occurs within 6 hours in water at 100°C (Selvig, 1977). This poorly described and conducted study offers limited utility in providing a measured hydrolysis rate. The test substance contains no functional groups generally recognized to readily undergo hydrolysis under neutral ambient conditions. Aromatic substituted bromo- groups are not readily cleaved, except by strong agents under forcing conditions, and ether groups are typically hydrolyzed by boiling in aqueous solutions of hydriodic acid (Fieser and Fieser, 1960). Strictly limited solubility of the test material further limits its ability to hydrolyze at an appreciable rate.

4.2.3 Fugacity

Level III fugacity modeling has been conducted on the test material using EPIWIN. The results indicate that the test substance will partition preferentially to soil and sediment. A calculated Henry's Law Constant of 4.25×10^{-7} atm-m^3/mol suggests that the test substance will not rapidly volatilize from water (in which it also has limited solubility). Volatilization from soil or sediment is also strictly limited. A water soil partition constant (Koc) of 71800 has been estimated using EPIWIN PCKOC. This high value indicates that the test substance possesses poor soil mobility.

4.3.4 Biodegradation

A study using adapted microorganisms showed that a commercial material containing Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo- (MC-680) was biodegraded < 1.41% after 211 days. Therefore, the material is not readily biodegraded (Calandra, 1976a).

4.3.5 Bioaccumulation

A bioconcentration study was conducted in carp exposed to 0.03 or 0.3 ppm Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo- for up to 8 weeks (CITI, 1976). The average bioconcentration factors (BCF) of the fish exposed to 0.03 ppm were 19.35, 24.65, 27.55 and 24.5 at 2, 4, 6, and 8 weeks, respectively. The average BCFs for 0.3 ppm were 41.6, 19.1, 6.0 and 8.6 and 17.85 at the same time points. These data suggest that the material initially concentrates in fish, but does not bioaccumulate over time. Some of the material in fish exposed to the high concentration (which is close to the solubility limit) is eliminated over time, and the concentration in the fish exposed to the lower concentration appears to reach steady-state. According to a classification scheme described by Franke et al. (1994), the BCF values calculated for Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo- suggest a low to moderate potential for bioconcentration in aquatic organisms.

4.3.6 Summary/Test Plan for Environmental Fate Parameters

Due to limited water solubility and potential to hydrolyze or volatilize, and due to preferential partitioning to soil or sediment (based on Level III Fugacity model predictions), Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo- will not be readily eliminated from the environment. The material is also not readily biodegraded, and has a low to moderate potential for bioconcentration in aquatic organisms. Sufficient environmental fate information is available to

adequately characterize environmental fate endpoints for screening purposes. No additional testing is necessary.

4.3 Ecotoxicity

4.3.1 Acute Toxicity to Fish

Three toxicity tests have been performed in fish (Wazeter and Goldenthal, 1974a,b; CITI, 1976). The 96-hr LC_{50} values for solubilized Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo- in trout, bluegill and orange-red killifish in these studies were 1410, 1531, and 230 mg/l, respectively. As the measured water solubility of the material at 25 degrees C is only 0.2 mg/l, it is obvious that test concentrations approaching the measured LC50 values (with solubilized material) will not be reached in the aquatic environment. The utility of EPIWIN ECOSAR (v0.99g) (with inputs of the CAS No. of the test substance and the measured values for melting point, water solubility and Log Pow given in Table 1) for estimating LC50 values in fish for this material is demonstrated by the calculation of an estimated 96-hr LC_{50} value of 43.51 mg/l, which is only approximately 5-times lower than the lowest experimental value for fish, but greater than the measured water solubility.

4.3.2 Acute Toxicity to Aquatic Invertebrates

There are no measured data to fill this endpoint. Acute toxicity for Daphnia and Mysid shrimp was estimated using EPIWIN ECOSAR (v0.99g). Inputs to the model were those used for fish (see above). The estimated 48-hr LC_{50} values for Daphnia and Mysid shrimp were 50.43 and 5.57 mg/l (respectively), which are greater than the measured water solubility. The 10-fold difference in the values obtained in these two species is likely due to a higher fat content in shrimp than Daphnia.

4.3.3 Acute Toxicity to Aquatic Plants

There are no measured data for this endpoint. Acute toxicity in algae was estimated using EPIWIN ECOSAR (v0.99g). Inputs to the model were the same as above for fish and Daphnia. The estimated 96-hr EC_{50} value obtained is 33.66 mg/l, which is again greater than the measured water solubility.

4.3.4. Summary/Test Plan for Ecotoxicity

Studies with solubilized Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo- show that the 96-hr LC_{50} values for trout, bluegill and orange-red killifish are several orders of magnitude higher than the natural solubility of the material in water. The 8-week lowest lethal concentration for carp (> 0.3 ppm) also is greater than the water solubility. Furthermore, since the test material tends to partition to soil and sediment (rather than water) and does not tend to leach from soil, material released into the environment is not expected to migrate to waterways. Therefore, concentrations of the test material that are acutely toxic to fish will not be reached in the aqueous environment.

No studies have been performed with aquatic invertebrates and algae. However ECOSAR values have been calculated (based on a measured Log Pow) that conservatively estimate the LC50 values for fish, Daphnia and Mysid shrimp, and the EC50 value for algae. All calculated values are several-fold higher than the measured water solubility. These data should be sufficient for screening purposes to indicate that the test substance is of low acute toxicity to aquatic organisms- even at levels approaching the solubility limit in water.

4.4 Human Health Data

4.4.1 Acute Mammalian Toxicity

This endpoint is filled by two sufficient oral toxicity studies in rats (Birdsall, 1972; Wazeter and Goldenthal, 1974c) and one in dogs (Wazeter and Goldenthal, 1974d), one inhalation study in rats (Wazeter and Goldenthal, 1974e), and two dermal toxicity studies in rabbits (Birdsall, 1972, x). The oral and dermal LD_{50} values were greater the highest concentrations tested (10000 mg/kg for oral and 2000 and 10000 mg/kg for dermal). The LD50 value for inhalation was greater than 36.68 mg/l. Higher concentrations could not be tested by inhalation due to the physical properties of the material.

Inhalation studies also have been performed on vapor from heating television rings containing FM680 to 135 °C (Horath and Goode, 1976), and pyrolysis products of ABS Resin/Sb_2O_3 (antimony) with and without FM680 (Wazeter and Goldenthal, 1975a,b). Results of the television ring study show that inhalation of 13.08 mg/l FM680 vapor for 4 hours did not cause death or abnormal pathology. Inhalation of material produced by pyrolysis of ABS Resin/FM680/Sb_2O_3 also did not cause death during a 4-hr exposure. However, these rats exhibited clinical signs during exposure such as decreased motor activity, eye squint, slight dyspnea and ocular porphyrin discharge. These symptoms resolved over 48 hours through 14 days. At necropsy, 2/10 animals exhibited scattered gray foci or congestion in the lungs. However, since the toxicological symptoms did not significantly differ from those exposed to ABS Resin/Sb_2O_3 without FM680, the symptoms were due to inhalation of pyrolysis products from ABS Resin and/or antimony, and not FM680.

4.4.2 Repeated Dose Mammalian Toxicity

A 106-day oral toxicity test in rats showed that ingestion of up to 1% Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo- in feed (for doses of approximately 792 mg/kg/day in males and 874 mg/kg/day in females) did not cause toxicity (Marias, 1977). Ingestion of 10% (for doses of approximately 8329 mg/kg/day in males and 9364 mg/kg/day in females) for 106 days was associated with hepatic changes in 10/10 males and 6/10 females. The lesions consisted of minimal focal of multifocal enlargement of hepatocytes within the centrilobular to midzonal regions. Other changes were not considered to be related to treatment. When ingested in the feed over a period of 14 days, a concentration of 10% did not produce toxicity (Wazeter and Goldenthal, 1975c).

Two studies were conducted to determine the toxicity and bromine content of tissues after administration of Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo- in feed for 28-days (Ohecs, 1972; Wazeter and Goldenthal, 1975d) . Whereas reduced body weight gains and

absolute and relative weights of some organs were observed in rats treated with 100 ppm (13.7 mg/kg/day) or 1000 ppm (138.5 mg/kg/day) in one study (Ohecs, 1972; Study 1), administration of 1000 ppm (75.2 mg/kg/day in males and 89.4 mg/kg/day in females) in a different study (Wazeter and Goldenthal, 1975d; Study 2) had no effect on the animals. The toxicological significance of the decreased body weight gains and organ weights in Study 1 is unclear since the body weight gains were only slightly depressed (and recovered after cessation of treatment), there were no corresponding changes in histopathology and clinical chemistry, and additional groups of treated animals did not have reduced body weight gains.

In rats treated with 100 or 1000 ppm in the diet for 28 days, bromine content of organs at termination was less than 1 ppm in all organs except fat (Study 1). Bromine content in fat varied between the two studies. Whereas a concentration of approximately 5 ppm was found in fat at termination of treatment with 1000 ppm in Study 2, 16.86 ppm bromine was found in fat from rats treated with 1000 ppm in Study 1. After 18 weeks of withdrawal, the bromine content of fat in rats treated with 1000 ppm in Study 2 was within normal limits (1.05 –1.79 ppm), but was slightly higher than control in Study 1 (3.41 ppm). These data suggest that the amount of test material ingested at the high dose in Study 1 was 10-fold higher than that of Study 2. This may account for the finding of toxicity in Study 1, but not in Study 2. Since concentrations of test material in the diets were not verified analytically, it is unknown whether the concentrations ingested were close to target.

A 21-day inhalation toxicity test in rats was performed with 5 and 20 mg/l micronized Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo- (Wazeter and Goldenthal, 1975e). The range of particle sizes was not listed; therefore the amount of material actually respired cannot be determined. None of the animals exposed to either concentration died. Findings attributable to administration of the test material were limited to the lungs (increased weight and foamy alveolar macrophages), and are common responses to inhalation of particulates. Based on the findings in the lungs, the NOAEL was < 5 mg/l.

Dermal toxicity of 50, 500 and 5000 mg/kg/day Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo- for 28 days has been tested in rabbits (Wazeter and Goldenthal, 1975f). There were no differences in hematological, biochemical or urinalysis parameters, organ weights or histopathology between treated and control animals. Diarrhea and weight loss occurring during the first 9 days of treatment in one high dose animal were not attributed to administration of test material. Erythema was observed in control as well as treated rats, suggesting that saline [rather than Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo- was the irritating material. Therefore, the NOAEL for Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo- in this study was set at 5000 mg/kg/day.

4.4.3 Genetic Toxicity

4.4.3.1 Mutagenicity

Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo- has been tested for mutagenicity in *S. typhimurium* strains TA98, TA100, TA1535, TA1537 and TA1538 in the absence and presence of a metabolic activation system (Brusick, 1976; Zeiger et al., 1987). Results of both studies were negative.

4.4.3.2 Chromosomal aberration

No existing study for chromosomal aberration has been identified. Testing for chromosomal aberrations is not necessary since the material is not well-absorbed by the GI tract (see below) and is not expected to produce chronic toxicity. In addition, repeated dose and developmental studies showed no adverse effects at fairly high doses, and the 106-day subchronic study showed no adverse effects on testes or ovaries.

4.4.4 Reproductive Toxicity

No mating studies with Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo- have been performed. The effect of ingestion of 0.1, 1 and 10% material in the diet for 106 days on pathology of reproductive organs in rats has been tested (Marias, 1977). The results show no effect of the test material on the testes, prostate, prostatic urethra and epididymis of males or the ovaries or uterus of females. Results of the developmental toxicity studies (see Section 4.4.5 below) indicate no effect of up to 10000 mg/kg/day test material during organogenesis on the number of resorptions, implantations, corpora lutea or viable or nonviable fetuses. Altogether, these results suggest that the potential for reproductive toxicity is low. Therefore, reproductive toxicity testing is not necessary

4.4.5 Developmental Toxicity

Data from two studies in rats show that Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo- is not a developmental toxicant at doses up to 10,000 mg/kg/day (Goldenthal 1978, 1979). This dose was not maternally toxic in one study, but was associated with an increased incidence of animals with a red vaginal discharge in the other. The significance of this finding is not clear, since there was no increase in post-implantation losses or differences in uterine condition between treated and control animals at cesarean section. . Existing studies are sufficient to fulfill the screening data needs for this endpoint, and no further testing is planned.

4.5 Additional Data

4.5.1 Pharmacokinetics

A pharmacokinetic study was conducted in which rats were given 0.05, 0.5 or 5% [^{14}C]FF-680 in feed for 1 day , or 0.05% for 10 days (Nomier et al., 1993). For the 1-day study, 99% of the recovered radioactivity was excreted in the feces within 96 hours. In the 10-day study, the cumulative amount of material excreted into the feces was approximately 87% of the recovered radioactivity. HPLC analyses showed that the feces contained only parent compound. At all dose levels, < 1% of the recovered radioactivity was found in the urine. In animals gavaged with 200 mg/kg test material, approximately 0.04% was excreted into bile within 6 hours. No radioactivity was detected in expired air from rats given 0.169% material for 24 hours. These results indicate that the vast majority of orally administered test material passes through the GI tract unabsorbed.

In animals given 0.05, 1.5 or 5.0% test material in the diet for 1 day, < 0.1 to 0.15% of the administered dose was found in the tissues that were collected. The only tissues containing detectable radioactivity in this study were thymus, adipose tissue and skin. In the 10-day feeding study, 4.8% and 0.17% of the administered dose was found in the GI tract and other organs, respectively. The highest percentage of the dose (0.06%) was found in adipose tissue, followed by kidney, skin, and thymus. All other tissues (blood, liver, heart, lung, brain, spleen, testes, and skeletal muscle) contained < 0.01% of the administered dose.

In a different study where rats were gavaged once after fasting with up to 4.97 mg/kg test material, 80% and 5% was excreted in feces and urine (respectively) within 96 hours (Diaz and Atallah, 1978). Approximately 2% of the radioactivity was present in all tissues 48 hours after treatment. A comparison of the residue levels found in liver (0.67 ppm) and kidneys (0.38 ppm) at 48 hours indicated that some of the material was eliminated through biliary excretion. Absorption of the material followed a two compartment system, with the first being blood and all tissues except fat, and the second consisting of fat. The rate constant for elimination was 0.02 and the half-life in blood was 36 hours. The half-lives in all tissues except fat averaged 4 days. Maximum residues present in any tissue were 0.05 ppm after 10 days except for fat (0.34 ppm). The low levels of FM-680 residues in tissues throughout the experiment suggested that the compound was poorly absorbed. However, a comparison of residue levels in liver and kidney indicated some elimination through biliary excretion. The residue levels in the fat showed that the material did not bioaccumulate (a negative bioaccumulation factor of 0.3x was observed).

A tissue residue accumulation/depletion study was conducted on a large number of male and female rats exposed to 1000 ppm Firemaster 680 in the diet for 24 weeks, followed by a 58-week recovery period (Industrial Bio-test Laboratories, Inc., 1979). The concentration of bromine in fat increased throughout the 24-week exposure period. Although a slight reduction of bromine in fat was noted after 12 weeks of recovery, the bromine concentration in fat of treated rats was four times that of control after 58 weeks of recovery. Although slight increases in the bromine concentration of liver, kidney and brain occurred during exposure, they decreased to levels found in controls after 2-4 weeks of recovery.

As shown previously (see Section 4.4.2), rats treated with 1000 ppm Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo- in the diet for a shorter time period (28 days) have increased bromine concentrations in fat after a recovery period of 18 weeks.

4.5.2 Skin and Eye Irritation

Adequate studies show that Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo- is not irritating to rabbit skin or eyes (Birdsall, 1972). The mother liquor for the manufacture of FM680 is slightly irritating to rabbit skin (Calandra, 1976b).

4.5.3 Sensitization

Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo- was not sensitizing to humans participating in a modified Draize multiple insult test (Wazeter and Goldenthal, 1974f). An additional test in the guinea pig showed that the mother liquor for the manufacture of Firemaster 680 was not sensitizing (Davis, 1976).

4.5.4 Human Experience

Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo- is not a sensitizer in humans (see above).

4.5.5 Summary/Test plan for mammalian toxicity

Adequate acute and repeated dose oral toxicity studies show ingestion of fairly large amounts of Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo- is required to produce toxicity. Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo- is also practically nontoxic by the oral route. Short-term inhalation of Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo- or vapors produced by heating materials containing Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo- to high temperature (i.e. simulating what may occur in a fire) is also well-tolerated. Repeated inhalation of an atmosphere containing respirable dust (5 mg/l) produces lung effects like those observed with similar concentrations of inert dusts. The material is also not irritating to the skin or eyes, and is not sensitizing to humans.

Adequate studies show that Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo- is not a mutagen or a developmental toxicant. Results of a long-term toxicity (90-day) test indicate that the material is not toxic to reproductive organs. The vast majority of the material passes through the GI tract unchanged after ingestion. Testing for chromosomal aberrations is not necessary for the reasons given in Section 5.

Results of the repeated dose oral, pharmacokinetic and residue accumulation studies show that small amounts of C14-labeled material and bromine are present in fat after several weeks of withdrawal from the material. Since repeated ingestion of large quantities of test material (100 to 1000 ppm) is well tolerated, the amount of test material and/or bromine that is sequestered in fat after these doses does not appear to be associated with toxicity.

5. Summary

In summary, valid data are present to satisfy all physical/chemistry, environmental and aquatic toxicity endpoints. Because the material has low water solubility and has a low propensity to distribute to water, estimated LC50 values calculated from EPIWIN/ECOSAR for Daphnia, Mysid Shrimp and algae are sufficient to characterize the toxicity in these species. Therefore, actual testing in these species is not necessary.

Existing studies on acute, repeated dose, genetic (mutations) and developmental toxicity are sufficient to satisfy these endpoints. Data for eye and skin irritation and sensitization are adequate (although not required). Testing for chromosomal aberrations and reproductive toxicity is not necessary since long-term (106-day) oral administration does not lead to reproductive organ toxicity, large doses are required to produce toxicity in rats, and the vast majority of an orally administered dose passes through the GI tract unabsorbed.

For developmental toxicity, the two existing studies are sufficient to fulfill the screening data needs for this endpoint, and no further testing is planned.

6. References

Birdsall JJ. 1972. WARF Institute, Inc. Report #2081295 for Michigan Chemical Corp., dated Sept. 11, 1972.

Brusick D. 1976. Mutagenicity Evaluation of 859-74-5: Final Report. Litton Bionetics, LBI Project #2547. Submitted to Michigan Chemical Corp., May 25, 1976.

Calandra JC. 1976a. Biodegradability study with 14C-tagged MC-680. Industrial Bio-Test Laboratories Inc. Report Number IBT 632-07189 to Michigan Chemical Corporation, dated Jun 11.

Calandra JC. 1976b. Primary skin irritation test with mother liquor 680 process, code No. 7-29-76-B in albino rabbits. Industrial Bio-Test Laboratories, Inc. Report #8530-09618, for Michigan Chemical Corp., dated Oct. 25, 1976.

Chemicals Inspection and Testing Institute, Japan (CITI). 1976. Measurement of the degree of accumulation of the test sample in fish body. Preliminary toxicity experiment. Testing period July 5, 1976 - Nov 5, 1976.

Diaz LI and Atallah YH. 1978. Pharmacokinetic study of FM-680 in rats. Velsicol Chemical Corp., Project #482348, dated Aug. 11, 1978.

Fieser LF and Fieser M. 1960. Organic Chemistry. D. C. Heath and Company, Boston, p. 137.

Franke C. et al. 1994. Chemosphere 29:1501-14.

Goldenthal EI. 1978. Pilot teratology study in rats: Compound FM 680. International Research and Development Corp., Project #163-544 for Velsicol Chemical Corporation, dated Mar. 2, 1978.

Goldenthal. 1979. Teratology study in rats. Compound FM 680. International Research and Development Corp., Study #163-547 for Velsicol Chemical Corp., dated Feb. 13, 1979.

Horath LL and Goode JW. 1976. Acute heated vapor inhalation toxicity study in rats. Industrial Bio-Test Laboratories, Inc. Report #8562-09787 to Michigan Chemical Corporation, dated Dec. 6, 1976.

Industrial Bio-Test Laboratories, Inc. 1979. Tissue residue accumulation/depletion study with Firemaster 680 in albino rats. Study #8532-08950, for Michigan Chemical Corporation, dated Jan. 9, 1979.

Kirk-Othmer Encyclopedia of Chemical Technology. 4th ed. 1993. New York, NY. John Wiley and Sons, Volume 10, page 961

Klimisch HJ, Andreae M and Tillmann U. 1997. A systematic approach for evaluating the quality of experimental toxicological and ecotoxicological data. Reg Tox Pharm 25:1-5.

Leo A, Hansch C and Elkins D. 1971. Partition coefficients and their uses. Chem Rev 71: 537-8.

Marias AJ. 1977. 90 day subacute oral toxicity study with Firemaster 680 in albino rats. Industrial Bio-Test Laboratories, Inc. Report #8532-08925, for Michigan Chemical Corportation, date Jan. 6, 1977.

Nomeir AA, Markham PM, Ghanayem BI and Chadwick M. 1993. Disposition of the flame retardant 1,2-bis(2,4,6-tribromophenoxy)ethane in rats following administration in the diet. Drug Metab Disp 21(2):209-214.

Ohecs P. 1972. Michigan Chemical Company 28 Day Rat Feeding Study. Sample 4884. WARF Institute, Inc., Report #2071960, dated Dec. 22, 1972.

Selvig C. 1977. Velsicol Chemical Corp., interoffice correspondence, Sept. 22, 1977.

Wazeter FX and Goldenthal EI. 1974a. Acute toxicity (TL50) study in the bluegill. International Research and Development Corp.Study #134-014, for Michigan Chemical Corp., dated Dec. 13, 1974.

Wazeter FX and Goldenthal EI. 1974b. Acute toxicity (TL50) study in the rainbow trout. International Research and Development Corp.Study #134-014, for Michigan Chemical Corp., dated Dec. 13, 1974.

Wazeter FX and Goldenthal EI. 1974c. Acute oral toxicity study in the albino rat. International Research and Development Corp. Report #134-011, for Michigan Chemical Corporation, dated Nov. 27, 1974.

Wazeter FX and Goldenthal EI. 1974d. Acute oral toxicity study in beagle dogs. International Research and Development Corp. Report #134-012, for Michigan Chemical Corporation, dated Nov. 27, 1974.

Wazeter FX and Goldenthal EI. 1974e. Acute inhalation study in the albino rat. International Research and Development Corp. Report #134-013, for Michigan Chemical Corporation, dated Nov. 27, 1974.

Wazeter FX and Goldenthal EI. 1974f. Modified Draize multiple insult test in male humans. International Research and Development Corp. Report #134-017, for Michigan Chemical Corporation, dated Jan. 30, 1975.

Wazeter FX and Goldenthal EI. 1975a. Acute inhalation study in the albino rat after pyrolysis. International Research and Development Corp. Report #134-038, for Michigan Chemical Corporation, dated March 12, 1975.

Wazeter FX and Goldenthal EI. 1975b. Acute inhalation study in the albino rat after pyrolysis. International Research and Development Corp. Report #134-039, for Michigan Chemical Corporation, dated March 12, 1975.

Wazeter FX and Goldenthal EI. 1975c. Fourteen day range finding study in rats: Compound Firemaster 680. International Research and Development Corp., Report #134-053, for Michigan Chemical Corp., dated Apr. 10, 1975.

Wazeter FX and Goldenthal EI. 1975d. Twenty eight day toxicity study in rats. International Research and Development Corp., Study #134-018 for Michigan Chemical Corporation, dated May 19, 1975.

Wazeter FX and Goldenthal EI. 1975e. Twenty-one day inhalation toxicity study in rats: Firemaster 680 (micronized). International Research and Development Corp., Report #134-016, for Michigan Chemical Corp.., dated Feb. 11, 1975.

Wazeter FX, and Goldenthal EI. 1975f. Twenty-eight day dermal toxicity study in rabbits. International Research and Development Corp., Study #134-015 for Michigan Chemical Corporation, dated Feb. 11, 1975.

Yu CC. 1979. Photolysis of Firemaster-680. Velsicol Chemical Corp. Laboratory Report, Project #484028, dated Jan. 23, 1979.

Yu CC and Atallah YH. 1977. Partition coefficients of MC-680, chlorendic anhydride and chlorendic acid. Velsicol Chemical Corp. Laboratory Report, Project #482348 - 484028, dated Dec. 16, 1977.

Yu CC and Atallah YH. 1978. Water solubility of several flame retardants and industrial chemicals. Velsicol Chemical Corporation Laboratory Report, Environmental Science Section, Project Number 484048, dated April 12, 1978.

Zeiger E, Anderson B, Haworth S, Lawlor T, Mortelmans K and Speck W. 1987. Salmonella mutagenicity tests. III. Results from the testing of 255 chemicals. Environ Mutagen 9 (Suppl 9): 1-110.

Test Plan Matrix for Benzene, 1,1'-[1,2-ethanediylbis(oxy)]bis[2,4,6-tribromo-

CAS No. 37853-59-1	Data Available	Data Acceptable	Testing Required
ENDPOINT	Y/N	Y/N	Y/N
PHYS/CHEM PROPERTIES			
Melting Point	Y	Y	N
Boiling Point	Y	Y	N
Vapor Pressure	Y	Y	N
Partition Coefficient	Y	Y	N
Water Solubility	Y	Y	N
ENVIRONMENTAL FATE			
Photodegradation	Y	Y	N
Stability in Water	Y	Y	N
Biodegradation	Y	Y	N
Transport between Environmental Compartments (Fugacity)	Y	Y	N
ECOTOXICITY			
Acute Toxicity to Fish	Y	Y	N
Acute Toxicity to Aquatic Invertebrates	Y	Y	N
Toxicity to Aquatic Plants	Y	Y	N
TOXICOLOGICAL DATA			
Acute Toxicity	Y	Y	N
Repeated Dose Toxicity	Y	Y	N
Genetic Toxicity-Mutation	Y	Y	N
Genetic Toxicity-Chromosomal Aberrations	N	NA	N
Toxicity to Reproduction	Y	Y	N
Developmental Toxicity	Y	Y	N

NA=Not Applicable